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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,846	04/20/2004	Steven R. Binder	02558B-063710US	5304
20350	7590	02/07/2007	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			WHALEY, PABLO S	
			ART UNIT	PAPER NUMBER
			1631	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/07/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/828,846	BINDER ET AL.
	Examiner Pablo Whaley	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 02 October 2006.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-31 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-31 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date _____	6) <input type="checkbox"/> Other: _____

## DETAILED ACTION

### CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-31, as they read on the species of systemic autoimmune disease (SLE) and antigens (Scl-70). Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied, as necessitated by amendment. They constitute the complete set presently being applied to the instant application.

### Claim Rejections - 35 USC § 103

Claims 1-5 and 11-31 are rejected under 35 U.S.C. 103(a) as being obvious by Zimmerman et al. (Electrophoresis, 1995, Vol. 16, p.941-947), in view of Thompson et al. (Lupus, 1993, 2, p.15-19) and Kim et al. (IEEE Transactions on Pattern Analysis and Machine Intelligence, 1986, p.761-765), and further supported by Anderson et al. (WO/1999/039298; Filed 03/02/1999).

Zimmerman et al. teach a computer-implemented method for identifying and classifying patient derived autoantibody data by discriminant analysis [Abstract]. More specifically, Zimmerman et al. teach the following aspects of the instantly claimed invention:

- Storing blot data obtained from patient serum with autoantibodies associated with known diseases in a computer database (i.e. memory) [Abstract and Sections 2.4.1 and 2.4.2], which is a teaching for a plurality of “reference data” sets as in claims 1 and 18.

- Blot data and scanned data representing levels associated with disease specific antibodies [Fig. 2 and 3A], as in claims 1 and 18.
- An integrated “Megablot” comprising values associated with myositis (left), myopathy (right) and neither (“0” values) [Fig. 3B, 3C, and 3D], which equates to a teaching for values that are associated with neither disease, as in claims 1 and 18.
- Comparison of blots of known groups to unknown samples using discriminate analysis [p.944, Col. 2, ¶ 2] and providing a statistically derived decision as output [p.945, Col. 2 and Table 1], as in claims 1 and 18.
- Computer system comprising software and hardware components for implemented the above process [Section 2.2 and 2.3], as in claims 18 and 22-24.
- Calculation of Chi-squared values (i.e. concordance value) and distance metric values (d') wherein mean known vectors are compared to unknown blot patterns [p.944, Col. 2, ¶ 3], as in claims 1, 11, 12, 14, 15, 18, 25, 26, 28, and 29. It is noted that “mean” is an implicit teaching for adding values and dividing by the total, as in claim 29.
- Discarding data if values exceed a certain distance value (i.e. cutoff value) [p.945, Col. 2 and Table 1], as in claims 13, 16, 27, and 30.
- Increasing said minimal distance and recalculating the analysis [p.945, Col. 2], which is an implicit teaching for a second threshold value as in claims 17 and 31.

Zimmerman et al. do not specifically teach the use of SLE antibody profiles and antigens (Scl-70), as recited in the claims 2-4 and 19-22 and the elected species. However, Zimmerman et al. suggest their procedure allows for diagnosis of other autoimmune diseases [Abstract]. Zimmerman et al. also do not specifically teach a “k-nearest neighbor” process, as in claim 11,

and 25-28. However, Zimmerman et al. suggest the use of other pattern recognition based on neural networks [p.947, Col. 1, ¶ 2].

Thompson et al. teach a method of patients with systemic lupus erythematosus (SLE) based on their autoantibody profile (Abstract). More specifically, Thompson et al. teach the following aspects of the instantly claimed invention:

- Reference autoantibody profiles related to the systemic autoimmune disease SLE [p.15, Methods and Table II]; as in instant claims 1 (lines 5-8), 2, 3, 18, and 19.
- Profile "Neg" representing a negative profile not associated with an SAD [Table I], which correlates to at least one reference data set associated with none of the SADs as in instant claim 1 (lines 8-9).
- Serum samples from 117 patients with levels for each of the autoantibody profiles [p.15, Materials and Methods], as in instant claim 1.
- Antibody profiles include SSA, SSB, centromere, Scl-70, Sm, nDNA, histone [Abstract], as in instant claims 4, 5, 20, and 21.

Kim et al. teach a fast k-nearest neighbor (kNN) search algorithm based on ordered partitions (Abstract). More specifically, Kim et al. teach the following:

- Applying the kNN search algorithm to identify test sample elements that are associated with training sample elements [p.761, Section II, Search Procedure]
- Determining a distance metric ( $r_i^2$ ) associating test and training data distances at various "node" level coordinate values [p.763, col. 1 (lines 1-19)]
- Distance threshold values  $d_k^2$  [p.763, col. 1 (lines 4-6)]

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the method of Zimmerman et al. using the SLE antibody profiles of

Thompson et al., and the added feature of a “k-nearest neighbor” algorithm taught by Kim et al., where the motivation would have been to improve automated diagnosis of SLE with a more robust statistical “kNN” procedure [Zimmerman et al., Section 4]. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the above teachings in view of Anderson et al., who teach a decision-support computer system using neural network algorithms to classify and identify patterns in antibody data for disease diagnosis [WO/1999/039298; Filed 03/02/1999, Summary of the Invention].

Claims 6-10 and 22-24 are rejected under 35 U.S.C. 103(a) as being obvious by Thompson et al. (Lupus, 1993, 2, p.15-19), in view of Kim et al. (IEEE Transactions on Pattern Analysis and Machine Intelligence, 1986, p.761-765) and Diamond et al. as applied to claims 1-5 and 11-14, above, and further in view of Kopecky (Design and Implementation of the Internet-Based Medical Expert System ToxoNet, 1999, p.1-153)

Applicant's arguments, filed 10/02/2006, that Thompson et al. fails to teach (i) storing a plurality of reference data sets in a memory, wherein reference data sets include a plurality of specific SADs, (ii) the concept of distinguishing patients with disease from patients without disease based on antibody patterns, and (iii) statistically derived decisions are not persuasive.

Regarding (i): In view of applicants' specie election, filed 12/27/2005, drawn to Specie A (SLE) and Specie B (Scl-70), prior art need not teach “a plurality” of specific reference data sets, but must teach reference data sets related to the elected species. The Examiner maintains that Thompson et al. indeed teach such limitations [Abstract and Table I], as well as a reference profile not associated with an SAD [Table I].

Regarding (ii): The Examiner maintains that Thompson et al. indeed teach determining correlations between antibody profiles and SLE [Table III], as required by the claims 1 and 18, as well as antibody profiles correlated to Sjogren's syndrome, which applicant has claimed is a specie of systemic autoimmune disease (instant claim 2).

Regarding (iii): The Examiner maintains that Thompson et al. indeed teach determining statistically derived decision [Tables III and IV], which is an implicit teaching for data being input into a computer for storage as in instant claims 1 and 18. Therefore this rejection is maintained for the reasons set forth above and reiterated.

Thompson et al., Kim et al., and Diamond et al. make obvious the method of identifying subsets of patients with systemic lupus erythmatosus (SLE) based on their autoantibody profile (Abstract), as set forth in the previous office action. The motivation to combine these references is re-stated for clarification. It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice automated diagnostic method of Thompson et al. using the k-nearest neighbor searching algorithm of Kim et al., where the motivation would have been to use a statistical analysis method designed to efficiently analyze large data sets, as taught by Kim et al. [Sections I and IV], resulting in the practice of the instant claimed invention. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the search algorithm of Diamond et al. with the computer implemented analysis of Thompson et al. in view of Diamond, who clearly teach a knowledge-based diagnostic system where clinical data and statistical analysis are used for automated diagnosis (Abstract).

Thompson et al., Kim et al., and Diamond et al. do not teach the limitation of transmitting data across a network to a remote computer, and displaying the output data.

Kopecky teaches an internet-based medical expert system (ToxoNet) for providing automated decision support to the clinician. ToxoNet consists of three parts: ToxoServer, ToxoBuilder, and ToxoApplet [Results Section]. ToxoServer stores and retrieves patient data from the database [Section 3.2.2]. Data is transmitted across a network to ToxoApplet [Fig. 3.3], which correlates to instant claims 8. ToxoApplet generates interpretive diagnostic reports displayed on a GUI [Fig. 5.3], which correlates to instant claims 6 and 7. ToxoNet decision graphs denote interpretive test results of patient data compared to IgM titer reference values [Fig. 2.5], which correlates to reference data sent over the network as in instant claims 9 and 10. Kopecky teaches the use of a computer system with input/output devices and memory [p.60], as well as a monitor and printer [p.123], as in instant claims 22-24.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the antibody profiles of Thompson et al. with the k-nearest neighbor searching algorithm of Kim et al. and the internet-based decision support system of Kopecky, where the motivation would have been to integrate autoimmune disease databases with a World Wide Web interface to provide remote automated decision support (Kopecky [1.1]), resulting in the practice of the instant claimed invention. One of ordinary skill in the art would have had a reasonable expectation of successfully combining the above teachings in view of Diamond et al., who teach an automated decision support system combining computer-implemented methods and analysis of immunological data sets [Abstract].

#### **Provisional Obviousness-Type Double Patenting Rejection**

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321 (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. 3.73(b).

Claims 1-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 7, 8, and 17 of co-pending Application No. 09/691,405. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the broadly encompassing scope of the instantly claimed invention causing the inventions to have overlapping embodiments. The instant claims and those of '405 recite the same method steps, with minor variations. For example, claims 1-3 of the instant application and claims 1-3 of co-pending Application '405 are directed to computer-implemented methods for identifying specific autoimmune diseases using a 'k-nearest neighbor' algorithm. It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the appropriate plurality of antibodies and then compare test data and stored reference data using said algorithm to identify disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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